Zika Virus

PlatformQHealth

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Zika Virus Overview

Zika Virus

- Single stranded RNA Virus
- Genus *Flavivirus*, Family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
- Transmitted to humans primarily by *Aedes (Stegomyia)* species mosquitoes

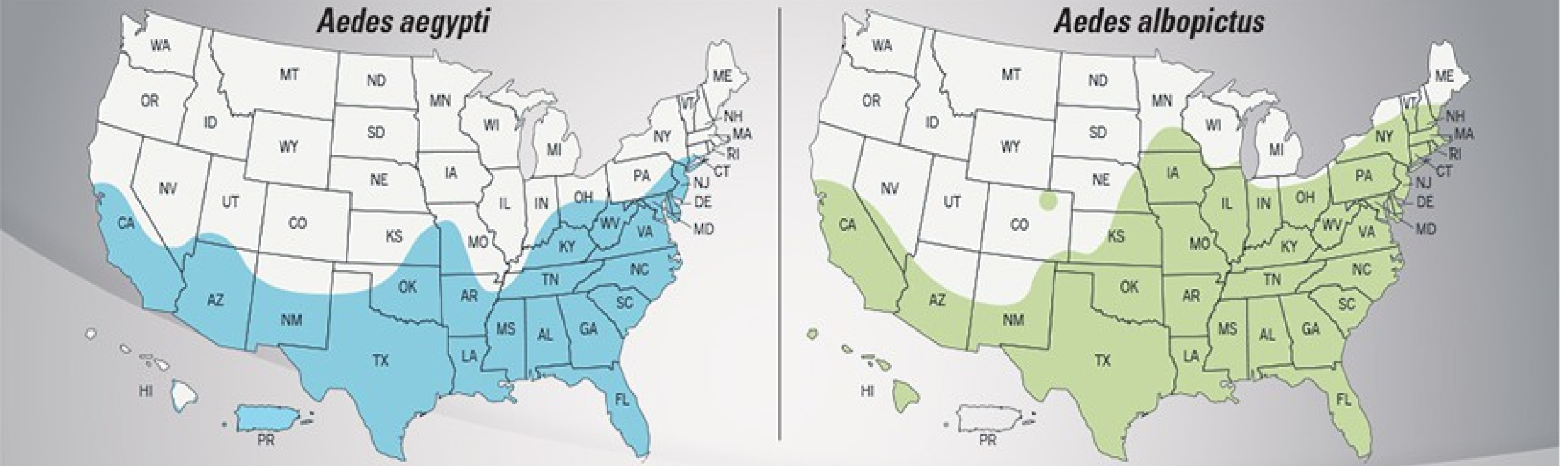
Zika Virus Vectors:
Aedes Mosquitoes

- *Aedes* species mosquitoes
  - Ae *aegypti* more efficient vectors for humans
  - Ae *albopictus*
- Also transmit dengue and chikungunya viruses
- Lay eggs in domestic water-holding containers
- Live indoors and outdoors
- Aggressive daytime biters; can also bite at night
- Prefer to bite people

***Aedes aegypti* mosquito**

***Aedes albopictus* mosquito**

Estimated range of *Aedes aegypti* and *Aedes albopictus* in the United States, 2016*



Aedes aegypti mosquitoes are more likely to spread viruses like Zika, dengue, chikungunya than other types of mosquitoes such as _Aedes albopictus_ mosquitoes.

- These maps show CDC's best estimate of the potential range of *Aedes aegypti* and *Aedes albopictus* in the United States.
- These maps include areas where mosquitoes are or have been previously found.
- Shaded areas on the maps do not necessarily mean that there are infected mosquitoes in that area.

**Maps have been updated from a variety of sources. These maps represent CDC's best estimate of the potential range of Aedes aegypti and Aedes albopictus in the United States. Maps are not meant to represent risk for spread of disease.*

SOURCE: Zika: Vector Surveillance and Control. www.cdc.gov/zika/vector/index.html

Other Modes of Transmission

- Maternal-fetal
- Intrauterine
- Perinatal

The Subcommittee on Arbovirus Laboratory Safety of the American Committee on Arthropod-Borne Viruses. Laboratory safety for arboviruses and certain other viruses of vertebrates. Am J Trop Med Hyg. 1980;29(6):1359-81.
European Centre for Disease Prevention and Control. Rapid risk assessment: Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome. Stockholm, Sweden: European Centre for Disease Prevention and Control; 2015.

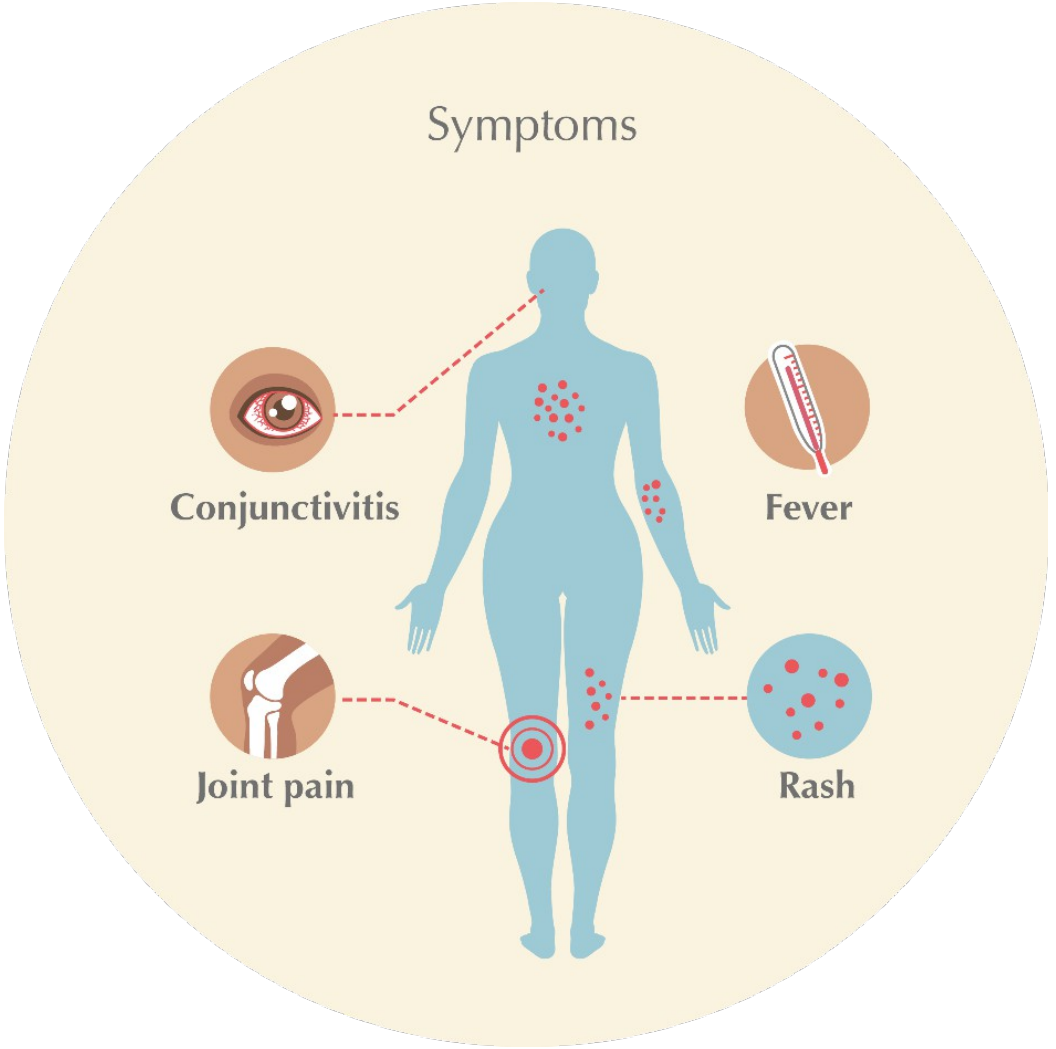
Zika Virus and Sexual Transmission

- Zika virus can be spread by a man to his sex partners

- Pregnant women with male partners who have or are at risk of Zika virus infection should abstain or use condoms for the duration of pregnancy

Zika Virus Disease Symptoms

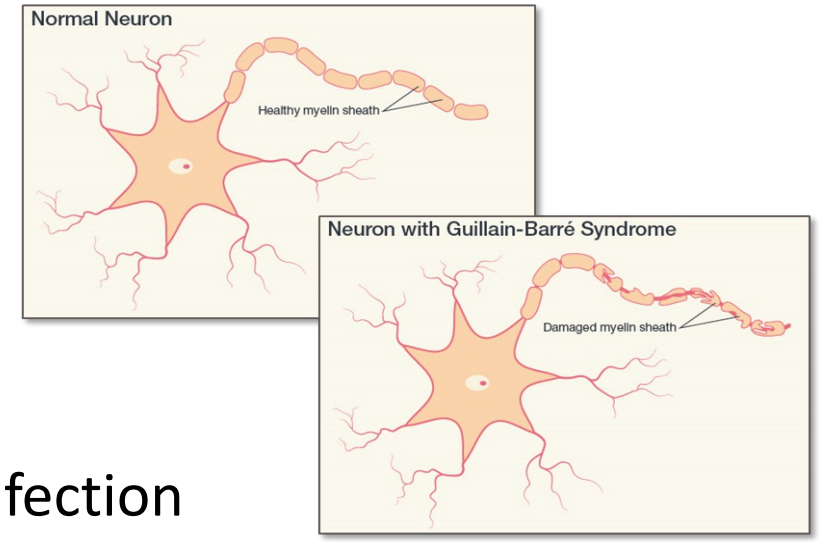
- Most common symptoms include:
  - Rash
  - Fever
  - Joint pain
  - Conjunctivitis (red eyes)
- Other symptoms include:
  - Muscle pain
  - Headache



Zika Virus Clinical Disease Course and Outcomes

- Clinical illness usually mild
- Symptoms last several days to a week
- Severe disease requiring hospitalization uncommon
- Fatalities are rare
- Guillain-Barré syndrome reported in patients following suspected Zika virus infection
  - Relationship to Zika virus infection under investigation

Complications of Zika Virus



- Guillain-Barré syndrome (GBS) has been reported

  after Zika virus infection, but causal link has not been established

  - Unclear how many people have had GBS after Zika virus infection
    - Brazil: 6 patients aged 2-57 years with neurologic syndromes (GBS and Acute Disseminated Encephalomyelitis) after Zika infection
    - French Polynesia: 38 cases of GBS, none among children
  - Overall, GBS incidence appears to increase with increasing age

European Centre for Disease Prevention and Control. Rapid risk assessment: Zika virus infection outbreak, French Polynesia. 14 February 2014. Stockholm: ECDC; 2014.
Minstério de Saúde. Protocolo de vigilância e resposta à ocorrência de microcefalia relacionada à infecção pelo vírus Zika 2015. http://portalsaude.saude.gov.br/images/pdf/2015/dezembro/09/Microcefalia---Protocolo-de-vigil--ncia-e-resposta---vers--o-1----09dez2015-8h.pdf
Sejvar J, Baughman A, Wise M, Morgan O. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36(2):123-33

Distinguishing Zika from Dengue and Chikungunya

- Dengue and chikungunya viruses transmitted by same mosquitoes with similar ecology
- Dengue and chikungunya can circulate in same area and rarely cause co-infections
- Diseases have similar clinical features
- Important to rule out dengue, as proper clinical management can improve outcome*

*WHO dengue clinical management guidelines: http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf

Zika Virus Epidemiology

- First isolated from a monkey in Uganda in 1947
- Prior to 2007, only sporadic human disease cases reported from Africa and southeast Asia
- In 2007, first outbreak reported on Yap Island, Federated States of Micronesia
- In 2013-2014, 28,000 cases reported from

*http://ecdc.europa.eu/en/publications/Publications/Zika-virus-French-Polynesia-rapid-risk-assessment.pdf

Zika Virus in Yap Island Outbreak

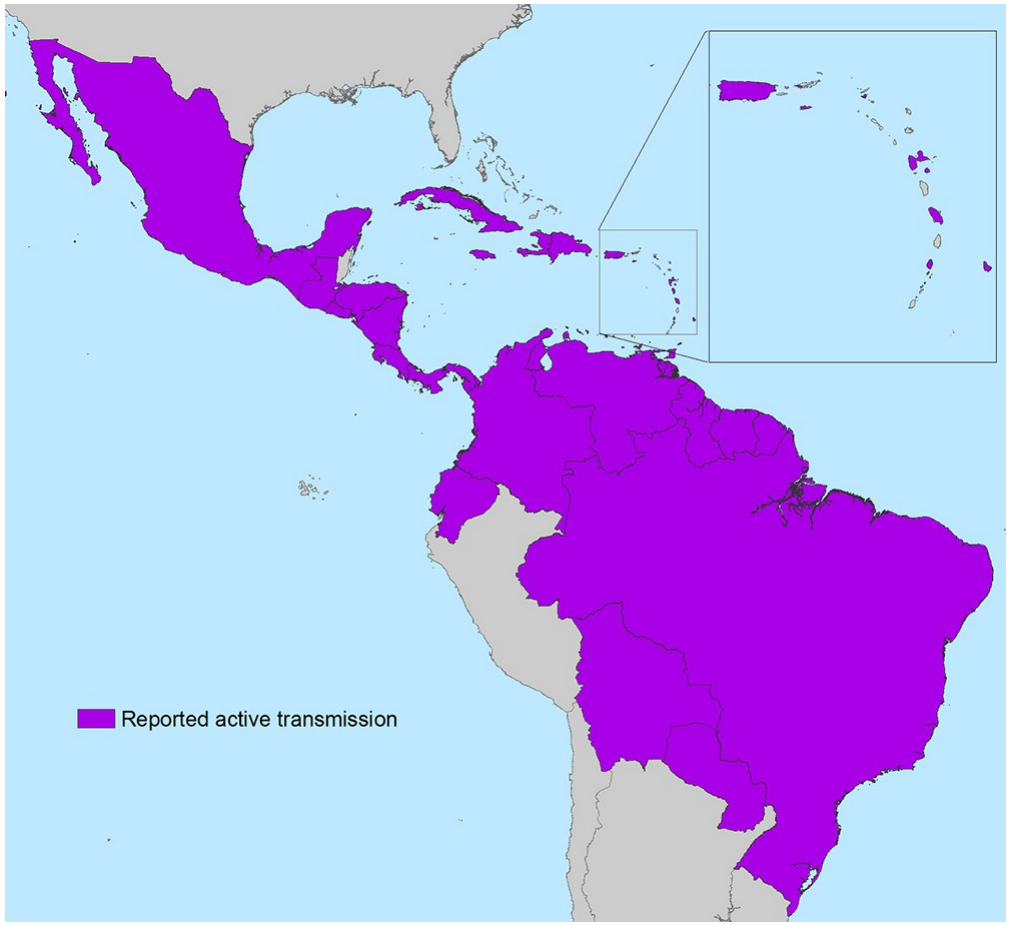
- Infection rate: 73% (95%CI 68–77%)
- Symptomatic attack rate among infected: 18% (95%CI 10–27%)
- All age groups affected
- Adults more likely to present for medical care

Duffy M. NEJM 2009

Zika Virus in the Americas

- In May 2015, the first locally-acquired cases in the Americas were reported in Brazil

- Currently, outbreaks are occurring in many countries or territories in the Americas, including the Commonwealth of Puerto Rico, the U.S. Virgin Islands, and American Samoa



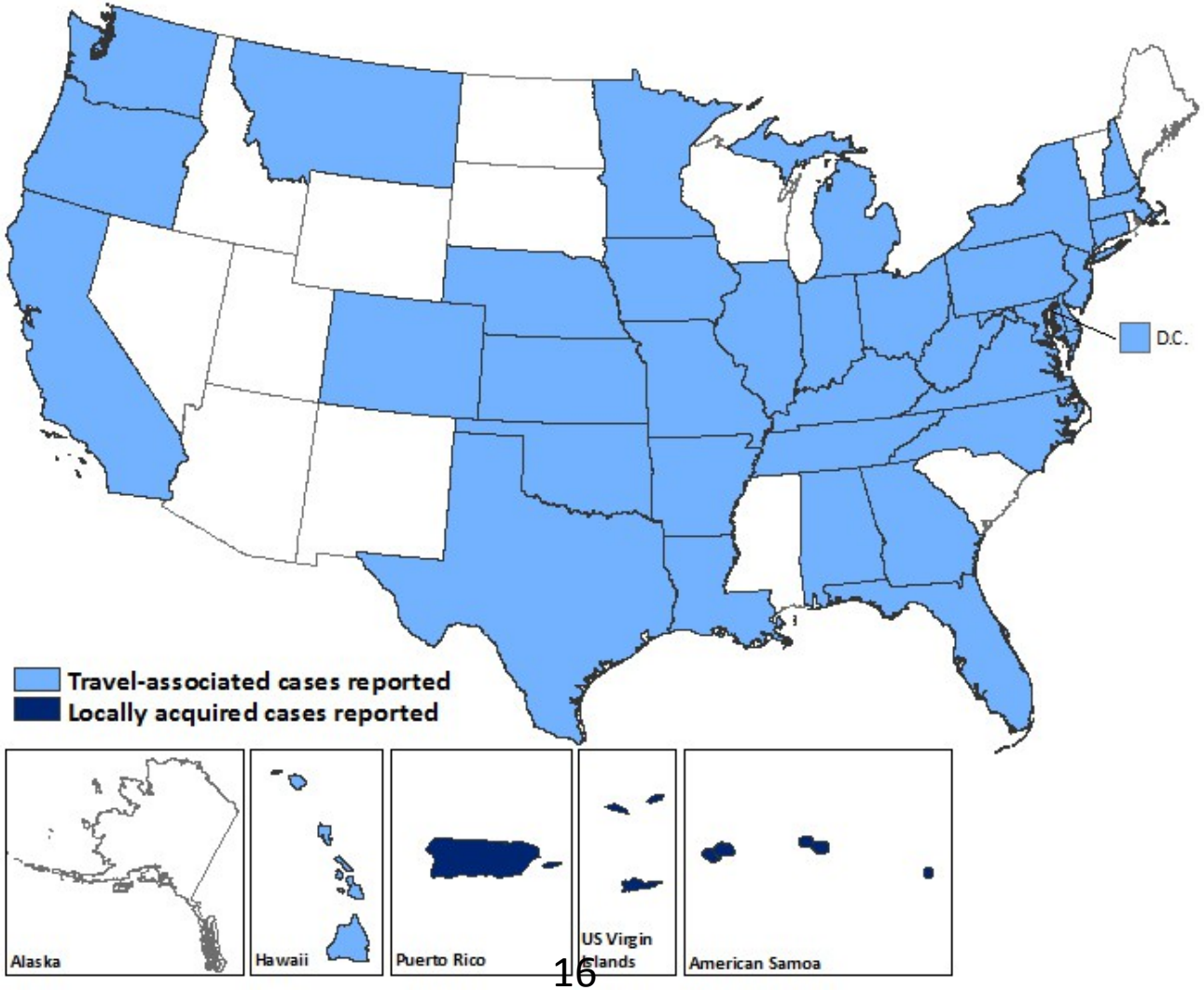
**Last updated March 22nd*

Zika Virus in the United States

- Local vector-borne transmission of Zika virus has not been reported in the continental United States
- With current outbreak in the Americas, cases among U.S. travelers will likely increase
- Imported cases may result in virus introduction and local transmission in some areas of U.S.

Zika Virus in the United States, 30 March 2016

- US States
  - 312 travel-associated cases
    - 27 pregnant women
    - 6 sexually transmitted
  - 0 locally-acquired vector-borne case
- US Territories
  - 3 travel-associated cases
  - 349 locally acquired cases
    - 37 pregnant women



Diagnostic Testing for Zika Virus

- Reverse transcriptase-polymerase chain reaction (RT-PCR) for viral RNA in serum collected ≤7 days after illness onset
- Serology for IgM and neutralizing antibodies in serum collected ≥4 days after illness onset
- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues
- More information about laboratory testing can be found at: http://www.cdc.gov/zika/state-labs/index.html

Serology Cross-Reactions with Other Flaviviruses

- Zika virus serology (IgM) can be positive due to antibodies against related flaviviruses (e.g., dengue and yellow fever viruses)
- Neutralizing antibody testing may discriminate between cross-reacting antibodies in primary flavivirus infections
- Difficult to distinguish infecting virus in people previously infected with or vaccinated against a related flavivirus
- Healthcare providers should work with state, territorial, and local health departments to ensure test results are interpreted correctly

Laboratories for Diagnostic Testing

- No commercially-available diagnostic tests
- Testing performed at CDC and a few state health departments
- CDC is working to expand laboratory diagnostic testing in states through the Laboratory Response Network (LRN)
- Healthcare providers should contact their state or territorial health department to facilitate diagnostic testing

Initial Assessment and Treatment

- No specific antiviral therapy
- Treatment is supportive (i.e., rest, fluids, analgesics, antipyretics)
- Suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya virus infections
- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage

Reporting Zika Virus Disease Cases

- Zika virus disease is a nationally notifiable disease
  - Healthcare providers are encouraged to report cases with laboratory evidence of Zika infection to their state, tribal, local, or territorial health department
- Health departments are requested to report cases with laboratory evidence of Zika infection to CDC
- Timely reporting allows health departments to assess and reduce the risk of local transmission or mitigate further spread

Zika Virus Preventive Measures in Puerto Rico

- No vaccine or medication to prevent infection or disease
- Primary prevention measure is to reduce mosquito exposure
- Protect infected people from mosquito exposure during first week of illness to prevent further transmission

Protecting Pregnant Women: Zika Prevention Kits (ZPKs)

- What's in a ZPK- Wave 1 for Puerto Rico?
  - Educational materials in English and Spanish
  - EPA-registered insect repellent
  - Condoms to reduce possible sexual transmission of Zika
  - Thermometer
  - Treatment tabs for preventing mosquitoes from breeding in standing water
  - Bed net

Zika Virus in Pregnant Women

Zika Virus in Pregnancy

- Limited information is available
- Existing data show:
  - No evidence of increased susceptibility
  - No evidence of more severe disease compared with non-pregnant people

Centers for Disease Control and Prevention, *CDC Health Advisory: Recognizing, Managing, and Reporting Zika Virus Infections in Travelers Returning from Central America, South America, the Caribbean and Mexico*, 2016.
Besnard, M., et al., Evidence of Perinatal Transmission of Zika Virus, French Polynesia, December 2013 and February 2014. Euro Surveill, 2014. 19(14): p. 1-5.
Oliveira Melo, A., et al., Zika Virus Intrauterine Infection Causes Fetal Brain Abnormality and Microcephaly: Tip of the Iceberg? Ultrasound in Obstetrics & Gynecology, 2016. 47(1): p. 6-7.

What is Microcephaly?

- Clinical finding of a small head when compared to infants of same sex and age
- Reliable assessment of intracranial brain volume
- Often leads to cognitive and/or neurologic issues
- Mechanisms
  - Primary due to abnormal development (often with a genetic etiology)
  - Secondary due to destruction of normally-forming brain tissue (by infection, vascular disruption)

Microcephaly Surveillance and Monitoring

- Difficult birth defect to monitor because of inconsistent definition and use of terminology
- Typically, in the US, below the third percentile on a standard growth chart identifies infants with microcephaly. However, standards can vary
  - CDC guidelines for evaluation and testing of infants with possible congenital Zika virus infection provide a standard case definition for microcephaly

Microcephaly and Zika

What we know

- Small number of positive test results for Zika virus infection in infants with microcephaly
- Microcephaly pattern consistent with Fetal Brain Disruption Sequence
  - Based on photos/scans of a small number of affected infants from Brazil
  - Retrospective investigation in French Polynesia outbreak in 2013-2014
  - Infants with other intrauterine infections such as cytomegalovirus

What we don't know

- Causal relation between Zika virus and microcephaly or other adverse pregnancy outcomes
- Full spectrum of phenotypes in affected infants
- Impact of timing of infection during pregnancy
- Impact of severity of maternal infection
- Magnitude of the possible risk of microcephaly and other adverse pregnancy outcomes

Pregnancy Outcomes and Zika Virus

- A range of other problems have been detected among fetuses and infants infected with Zika virus before birth including:
  - Absent or poorly developed brain structure
  - Defects of the eye
  - Impaired growth

- Although Zika has been linked with birth defects and other problems in infants, there is more to learn

- Researchers are collecting data to better understand the impact of Zika on mothers and their children

CDC Recommendations: Pregnant Women Considering Travel

- Pregnant women in any trimester should consider postponing travel to areas where Zika is present

- Pregnant women who do travel to one of these areas should talk to their healthcare provider and strictly follow steps to avoid mosquito bites during the trip

Evaluating Pregnant Travelers

- **Recommendations**
  - Ask pregnant women about travel history.
  - If history of travel to an area with ongoing Zika virus transmission during pregnancy, evaluate for symptoms of and test for Zika virus infection.
  - Pregnant women with male partners who have Zika virus infection or potential Zika virus exposure should use condoms or abstain from sexual activity for the duration of pregnancy.

CDC Recommendations:
Testing for Asymptomatic Pregnant Women with Possible Zika Virus Exposure

- Serologic (IgM) testing can be offered to asymptomatic pregnant women

- Negative IgM result could suggest a recent infection did not occur and obviate need for serial ultrasounds

- Information about performance of testing of asymptomatic persons limited

Zika Virus Disease Prevention: Pregnant Women

- CDC recommends taking the following steps to prevent mosquito bites:
  - Use EPA-registered insect repellents, including DEET and permethrin
  - Wear long-sleeved shirts and pants to cover exposed skin
  - Stay and sleep in screened-in or air-conditioned rooms
  - Wear permethrin-treated clothes
  - Practice mosquito prevention strategies indoors and outdoors throughout the entire day

- Pregnant women with male partners who have Zika virus infection should take the following measures to prevent sexual transmission:

Areas With Ongoing Zika Virus Transmission:
Evaluating Pregnant Residents

- Healthcare providers should
  - Evaluate for symptoms of Zika virus infection
  - Perform appropriate testing according to CDC's guidelines
- Local health officials should determine when to implement testing of asymptomatic pregnant women based on levels of Zika transmission and laboratory capaticy
- Recommendations
  - Offer serologic testing at
    - Initiation of prenatal care
    - Follow up mid-2nd trimester
  - Routine ultrasound screening recommended for all pregnant women at 18–20 weeks of gestation

CDC

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
February 5, 2016

Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016

Titilope Oduyebo, MD[1,2]; Emily E. Petersen, MD[2]; Sonja A. Rasmussen, MD[3]; Paul S. Mead, MD[4]; Dana Meaney-Delman, MD[5]; Christina M. Renquist, MPH[6]; Sascha R. Ellington, MSPH[2]; Marc Fischer, MD[4]; J. Erin Staples, MD, PhD[4]; Ann M. Powers, PhD[4]; Julie Villanueva, PhD[4]; Romeo R. Galang, MD[1,7]; Ada Dieke, DrPH[1,2]; Jorge L. Muñoz, PhD[4]; Margaret A. Honein, PhD[6]; Denise J. Jamieson, MD[2]

On February 5, 2016 this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

CDC has updated its interim guidelines for U.S. health care providers caring for pregnant women during a Zika virus outbreak (*1*). Updated guidelines include a new recommendation to offer serologic testing to asymptomatic pregnant women (women who do not report clinical illness consistent with

Evidence suggesting an association of Zika virus infection with an increased risk for congenital microcephaly and other abnormalities of the brain and eye (*5*) prompted the World Health Organization to declare the Zika virus outbreak a Public Health Emergency of International Concern on February 1, 2016 (http://www.who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en/).

Acute Zika Virus Disease in Infants and Children

Clinical Manifestations of Zika Virus in Children

- Most children asymptomatic or have mild illness
- Zika virus outbreak in Yap Island, Micronesia, 2007
  - Illness reported in persons 1-76 years of age
  - Most common signs and symptoms: rash (macular or papular), fever, arthralgia, conjunctivitis
  - Children 0-19 years had lower attack rates than adults 20-59 years
- Among 8 travel-related cases of Zika virus disease in children in US
  - All had rash and at least one additional manifestation (fever, arthralgia, and nonpurulent conjunctivitis)

Duffy MR, Chen TH, Hancock WT, Powers AM, Kool JL, Lanciotti RS, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. The New England journal of medicine. 2009 Jun 11;360(24):2536-43
CDC unpublished data, 2016

Zika Virus Laboratory Testing of Infants

- Recommended for
  1. Infants with microcephaly or intracranial calcifications born to women who resided in an area with Zika virus transmission while pregnant
  2. Infants born to mothers with positive or inconclusive test results for Zika virus infection

Infants without microcephaly or intracranial calcifications whose mothers traveled to or resided in areas with ongoing Zika transmission during pregnancy but were not tested

- If infant has normal head circumference, prenatal ultrasounds, postnatal ultrasounds (if performed), physical examination → routine care

- Use clinical judgment if an infant has abnormalities other than microcephaly or intracranial calcifications
  - Consider testing mother before infant

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 65
February 19, 2016

Update: Interim Guidelines for Health Care Providers Caring for Infants and Children with Possible Zika Virus Infection — United States, February 2016

Katherine E. Fleming-Dutra, MD[1]; Jennifer M. Nelson, MD[2,3]; Marc Fischer, MD[4]; J. Erin Staples, MD, PhD[4]; Mateusz P. Karwowski, MD[2,5]; Paul Mead, MD[4]; Julie Villanueva, PhD[6]; Christina M. Renquist, MPH[7]; Anna A. Minta, MD[2,8]; Denise J. Jamieson, MD[9]; Margaret A. Honein, PhD[7]; Cynthia A. Moore, MD, PhD[7]; Sonja A. Rasmussen, MD[10]

CDC has updated its interim guidelines for U.S. health care providers caring for infants born to mothers who traveled to or resided in areas with Zika virus transmission during pregnancy and expanded guidelines to include infants and children with

Americas as of February 17, 2016 (http://www.cdc.gov/zika/geo/active-countries.html). In October 2015, a marked increase in the number of infants with microcephaly was reported in Brazil (5). Because of the temporal and geographic occurrence of Zika

CDC Activities and Plans

CDC Response to Zika

CDC Activities and Plans

- Very little is known about the risks of Zika virus infection during pregnancy
- Increased understanding of the impact of Zika virus infection on pregnant women and their infants is needed
- To learn more about the impact of Zika virus infection during pregnancy, CDC is collaborating with state, tribal, local, and territorial health departments to collect information about women infected with Zika virus during pregnancy and their infants
- The information collected will:
  - Direct public health efforts intended to mitigate the impact of Zika virus infection
  - Guide recommendations for the monitoring and treatment of women affected by Zika during pregnancy

Zika Pregnancy Surveillance

- In collaboration with state and territorial health departments, CDC has established two surveillance systems for pregnant women with Zika virus infection
  - US Zika Pregnancy Registry
    - 50 U.S. States & Washington, DC
  - Zika Active Pregnancy Surveillance System (ZAPSS)
    - Puerto Rico
    - Data collected via medical record abstraction
- Surveillance systems will facilitate public health response for pregnant women with

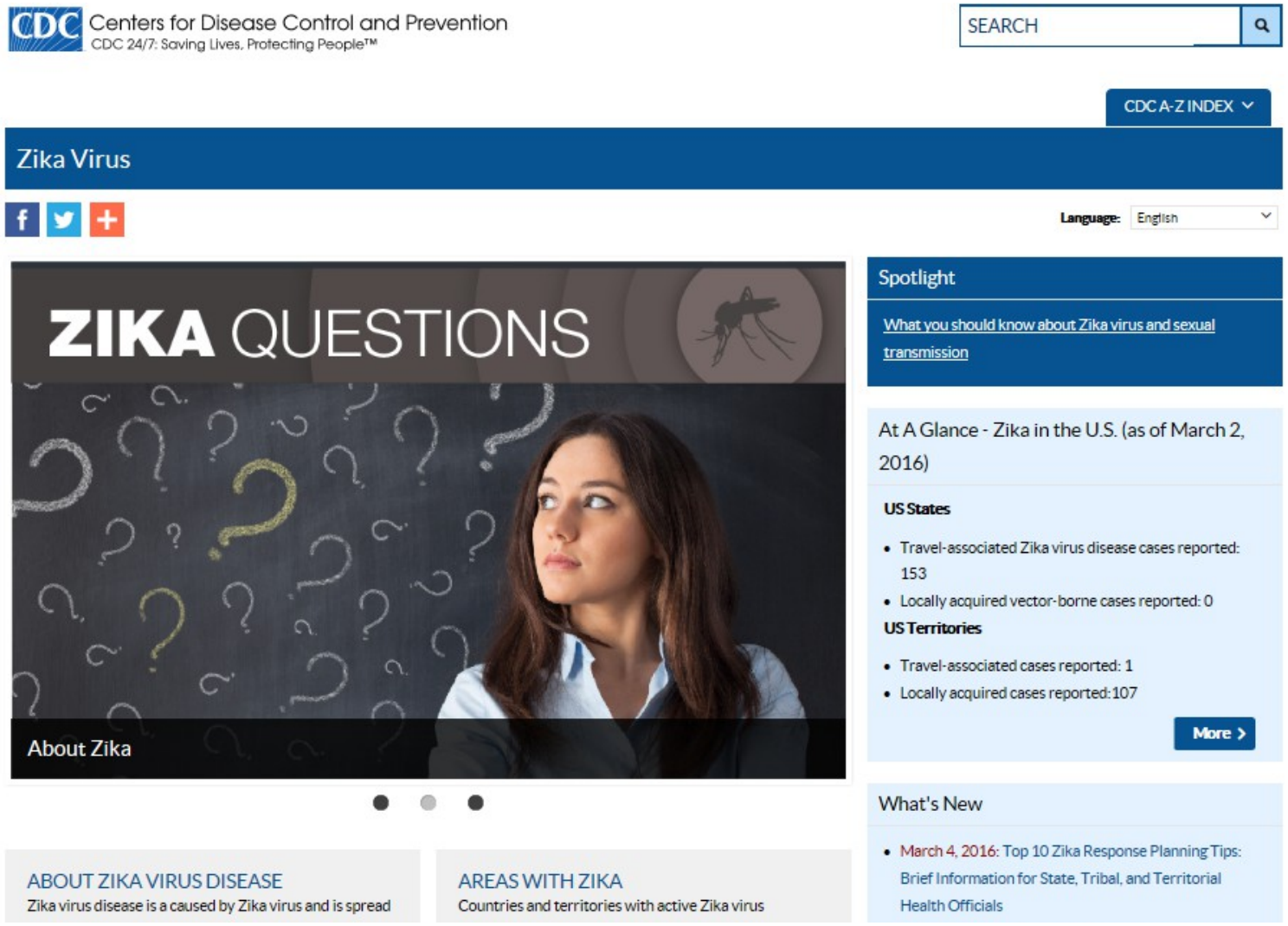
Clinical Inquiries Hotline

- Call the CDC Emergency Operations Center Watch Desk at 770-488-7100 and ask for the Zika Pregnancy Hotline
- Email ZikaMCH@cdc.gov.

Summary

- Zika virus continues to circulate and cause locally-transmitted disease in the Americas
- Consider the possibility of Zika virus infection in travelers with acute fever, rash, arthralgia, or conjunctivitis within 2 weeks after return
- A substantial increase in rates of congenital microcephaly have been reported in Brazil
  - Research is underway to characterize the relationship between Zika and congenital microcephaly
- Pregnant women in any trimester should consider postponing travel to areas of Zika virus transmission

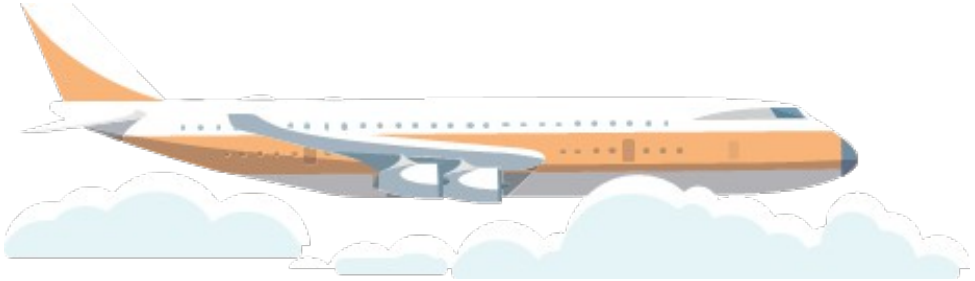
www.cdc.gov/zika



Additional resources

- CDC Zika virus information: http://www.cdc.gov/zika/
- PAHO Zika virus pages: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=427&Item
- Zika virus information for clinicians: http://www.cdc.gov/zika/hc-providers/index.html
- Zika virus information for travelers and travel health providers: http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/
- Travel notices: http://wwwnc.cdc.gov/travel/notices

Zika Travel Information



For the most current information about Zika virus, please visit www.cdc.gov/zika.

Zika Travel Notices

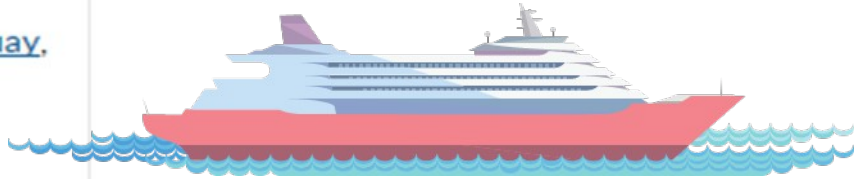
- Zika Virus in Cape Verde
- Zika Virus in Mexico
- **The Caribbean**

  Currently includes: Aruba; Barbados; Bonaire; Cuba; Curaçao; Dominica; Dominican Republic; Guadeloupe; Haiti; Jamaica; Martinique; the Commonwealth of Puerto Rico, a US territory; Saint Martin; Saint Vincent and the Grenadines; Sint Maarten; Trinidad and Tobago; US Virgin Islands
- **Central America**

  Currently includes: Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama
- **The Pacific Islands**

  Currently includes: American Samoa, Marshall Islands, New Caledonia, Samoa, Tonga
- **South America**

  Currently includes: Bolivia, Brazil, Colombia, Ecuador, French Guiana, Guyana, Paraguay, Suriname, Venezuela
- 2016 Summer Olympics (Rio 2016)



Thanks to our many collaborators and partners!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Back up slides

Pregnancy Outcomes and Zika Virus

- Pregnant woman residing in Brazil
  - Symptoms of Zika virus disease at 10 weeks
- Ultrasound findings
  - 22 weeks: Fetal mild hypoplasia of cerebellar vermis and head circumference <10th percentile
  - 25 weeks: Fetal microcephaly (head circumference <3rd percentile) with severe hypoplasia of cerebellar vermis, enlargement of posterior fossa, normal brain parenchyma
- Testing
  - 28 weeks: Amniotic fluid positive for Zika virus RNA; serum and urine negative by Zika RT-PCR
- Delivery
  - Infant born with severe ventriculomegaly, microphthalmia, cataracts and severe arthrogryposis

Calvet Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study. Lancet Infect Dis 2016. Epub February 17, 2016.

Pregnancy Outcomes and Zika Virus

- Pregnant woman residing in Brazil
  - Symptoms of Zika virus disease at 18 weeks
- Ultrasound findings
  - 16 weeks: Normal
  - 21 weeks: Fetal microcephaly with moderate ventriculomegaly and partial agenesis of the cerebellar vermis
  - 27 weeks: Fetal microcephaly with ventricular dilation, asymmetry of hemispheres, hypoplastic cerebellum and absence of cerebellar vermis
  - 40 weeks: Fetal microcephaly with calcifications
- Testing
  - 28 weeks: Amniotic fluid positive for Zika virus RNA, serum and urine negative by Zika RT-

Calvet Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study. Lancet Infect Dis 2016. Epub February 17, 2016.

Pregnancy Outcomes and Zika Virus

- Two pregnant women in Brazil had clinical signs of Zika during first trimester
- Infants born with microcephaly at 36 and 38 weeks gestation
  - Died within 20 hours of birth
- Zika virus RNA detected in brain tissue of both infants
- Significant histopathologic changes in the brain
  - Parenchymal calcification and necrosis

Martines RB, Bhatnagar J, Keating MK, et al. *Notes from the Field*: Evidence of Zika Virus Infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses — Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65(Early Release):1–2.

Pregnancy Outcomes and Zika Virus

- Two additional women in Brazil had clinical signs of Zika during the first trimester
  - Two fetal losses at 11 & 13 weeks gestation
- Zika virus RNA detected in products of conception
- Zika viral antigen detected by immunohistochemistry in one case
- Histopathologic changes in one case
  - Calcification and fibrosis in the chorionic villi

Martines RB, Bhatnagar J, Keating MK, et al. *Notes from the Field*: Evidence of Zika Virus Infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses — Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65(Early Release):1–2.

Pregnancy Outcomes and Zika Virus

- Pregnant woman residing in Brazil from preconception until 29 weeks of gestation
  - Symptoms of Zika virus disease at 13 weeks
- Ultrasound findings
  - 14 & 20 weeks: normal fetal growth & anatomy
  - 29 weeks: evidence of fetal anomalies
  - 32 weeks: intrauterine growth restriction, microcephaly, and other brain abnormalities
- Termination at 32 weeks
  - Brain weight 4 SD below normal
  - Zika virus RNA detected in fetal brain tissue

Mlakar J, Korva M, Tul N, et al. *Zika Virus Associated with Microcephaly*. NEJM 2016 Feb 10.

Women of Reproductive Age Residing in Areas of Ongoing Zika Virus Transmission

- *For women who do not desire pregnancy*, provide counseling on
  - Correct and consistent use of effective contraception
  - Condoms to reduce risk of contracting sexually transmitted infections

Recommended Zika Virus Testing for Infants*

- Recommended tests
  - Zika virus RNA (RT-PCR), IgM, and neutralizing antibodies
  - Dengue virus IgM and neutralizing antibodies
- Clinical specimens
  - Serum (umbilical cord or direct, within 2 days of birth if possible)
  - Cerebrospinal fluid, if obtained for other studies
- Consider histopathologic evaluation (placenta and umbilical cord)
  - Zika virus immunohistochemical staining (fixed tissue)
  - Zika virus RT-PCR (fixed and frozen tissue)
- Additionally, if not already performed, test mother's serum

Evaluation and Testing for All Infants with Possible Congenital Zika Virus Infection

For all infants with possible congenital Zika virus infection, perform the following:

- Thorough physical examination, including careful measurement of the head circumference, length, weight, and assessment of gestational age*
- Cranial ultrasound, unless prenatal ultrasound results from third trimester demonstrated no abnormalities of the brain
- Further evaluation
  - neurologic abnormalities, dysmorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions*
  - hearing by evoked otoacoustic emissions testing or auditory brainstem response testing, either before discharge from the hospital or within 1 month after birth*
  - eye exam to include visualization of the retina, optic nerve, and macula either before discharge from the hospital or within 1 month after birth*
- Other evaluations specific to the infant's clinical presentation

*If any abnormalities are noted, consultation with the appropriate specialist is recommended.

Additional Evaluation for Infants with Microcephaly or Intracranial Calcifications

- For infants with microcephaly, consultations are recommended with
  - A clinical geneticist or dysmorphologist
  - A pediatric neurologist to determine appropriate brain imaging and additional evaluation (e.g., US, CT scan, MRI, and/or EEG)
  - A pediatric infectious disease specialist should be considered after testing for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus, lymphocytic choriomeningitis virus, and herpes simplex viruses
- Further testing includes
  - Complete blood count, platelet count, and liver function tests including alanine aminotransferase, aspartate aminotransferase, and bilirubin
- Consideration of genetic and other teratogenic causes based on additional congenital anomalies that are identified through clinical examination and imaging studies

Recommended Long-Term Follow-up of Infants with Possible Congenital Zika Virus Infection

- Report case to state, territorial, or local health department and monitor for additional guidance as it released
- Conduct additional hearing screen at age 6 months, plus any appropriate follow-up of hearing abnormalities detected through newborn hearing screening
- Carefully evaluate head circumference and developmental characteristics and milestones throughout the first year of life
  - Use of appropriate consultations with medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy)

Recommended Testing for Acute Zika Virus Disease

- Test serum and, if obtained for other reasons, cerebrospinal fluid
  - If symptoms present for <7 days
    - Zika virus RNA by RT-PCR
  - If Zika virus RNA is not detected and symptoms have been present for ≥4 days
    - Zika and dengue virus IgM and neutralizing antibodies

- More information about laboratory testing can be found at: http://www.cdc.gov/zika/state-labs/index.html

Laboratory Evidence of Zika Virus Infection

- Positive test results
  - In any clinical sample
    - Zika virus by culture, RNA by RT-PCR, or antigen
    - Zika virus IgM with confirmatory neutralizing antibodies ≥ 4-fold higher than dengue virus neutralizing antibodies
- Inconclusive result
  - Zika virus neutralizing antibodies < 4 fold higher than dengue

Clinical Management

- No specific antiviral treatment
- Supportive care
- Avoid nonsteroidal anti-inflammatory drugs (NSAIDs) until dengue virus ruled out and in children <6 months
- Avoid aspirin in children with suspected viral infection due to the association with Reye's syndrome

Guidelines for Breastfeeding for Mothers with Zika Virus Infection and Living in Areas with Zika virus

- Zika virus RNA has been identified in breast milk
- Zika virus has not been cultured from breast milk
- No cases of Zika transmission associated with breastfeeding have been reported
- Mothers are encouraged to breastfeed their infants
- Current evidence: benefits of breastfeeding outweigh theoretical risks

Prevention of Zika Virus in Infants and Children

- Mosquito prevention
  - Air conditioning or window and door screens when indoors
  - Long-sleeves and long pants
  - Use permethrin-treated clothing and gear
  - When use as directed on the product label, most EPA*-registered insect repellants can be used in children ≥ 2 months
  - Oil of lemon eucalyptus should not be used in children < 3 years old
  - Mosquito netting for carriers, strollers, or cribs for infants

*EPA= Environmental Protection Agency

Nasci, RS et al. Protection against Mosquitoes, Ticks, & Other Arthropods in Chapter 2: The Pre-Travel Consultation: Counseling & Advice for Travelers http://wwwnc.cdc.gov/travel/yellowbook/2016/the-pre-travel-consultation/protection-against-mosquitoes-ticks-other-arthropods

Prevention of Zika Virus Infection in Infants and Children

- Healthcare providers should educate parents and caregivers about mosquito bite prevention in infants and children if they are traveling to or residing in areas affected by Zika virus

- Parents should protect infants and children with Zika virus from mosquito bites for at least one week to decrease risk of transmission to others